

Baby Badger Network ECHO

Case Recommendation Summary

Session Date: Friday, October 20, 2024

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Case Summary

A compilation of mostly NICU (some PICU) cases were presented. These cases highlighted a recurring theme of recommendation for genetic testing (e.g., single gene analysis, panel etc) following negative rapid exome or genome.

The presenter sought guidance regarding:

- *When is Whole Genome Sequencing (rapid, inpatient) indicated after negative Whole Exome Sequencing (rapid, inpatient)*
- *How do we navigate the decision whether to continue testing after negative ES/GS? How do we weigh apparently opposing considerations of continuing to search for answers with being good stewards of healthcare resources and diminishing diagnostic yield?*

There are no clear guidelines in these situations. Some things to consider:

- Seek guidance from the test lab to advise. You may learn that...
 - The coverage may have been less than optimal, but still “good enough”
 - There are no other available clinical test options to find the answer
 - The region is a “hot spot” (more likely to mutate than other regions due to GC rich content for example) and perhaps Sanger sequencing may be helpful
 - The lab can look at raw data to provide more insight
- A clinical diagnosis can be made in the absence of a molecular diagnosis when a strong suspicion for the specific diagnosis exists and other supporting information exists (imaging, biochemical labs, family history, etc.)

There are many genes that do not have good coverage given the short-read sequencing technology used for WES and some WGS. Future technologies using long read sequencing may help with this issue.

- **Other molecular technologies are being developed that may help with diagnosis in the setting of a negative exome or genome such as Episign (evaluating the methylation of certain genes). Testing laboratories may have helpful advice about the use of these emerging tests in your specific case presentation.**
- These patients may make good candidates for Undiagnosed Disease Programs that have other molecular testing tools available including long read sequencing.